Claims

1. A method for increasing the mitogenesis, survival, growth, or differentiation of a cell, said method comprising administering a NRG-2 polypeptide to said cell in an amount effective for increasing the mitogenesis, survival, growth, or differentiation of said cell, wherein said cell expresses an erbB receptor that is selective for a NRG-2 polypeptide.

2. The method of claim 1, wherein said erbB receptor is selected from the group consisting of an erbB4 homodimer, an erbB2/erbB4 heterodimer, and an erbB1/erbB3 heterodimer.

3. The method of claim 1, wherein said cell is selected from the group consisting of a neuronal cell and a neuronal progenitor cell.

4. The method of claim 1, wherein said cell is a neuronal-associated cell.

5. The method of claim 4, wherein said neuronal-associated cell is selected from the group consisting of a Schwann cell, an astrocyte, an oligodendrocyte, an O-2A progenitor cell, a glial cell, a microglial cell, an olfactory bulb ensheathing cell, and a sensory organ cell.

6. The method of claim 1, wherein said cell is a muscle cell.

7. The method of claim 6, wherein said muscle cell is selected from the group consisting of a myoblast, a satellite cell, a myocyte, a skeletal muscle cell, a smooth muscle cell, and a cardiac muscle cell.

8. A method of stimulating mitogenesis of a glial cell, said method comprising contacting said glial cell with a recombinant NRG-2 polypeptide.

9. The method of claim 8, wherein said glial cell is selected from the group consisting of oligodendrocytes, microglia, myelinating glia, an olfactory bulb ensheathing cell, and glial cells in an adult.

10. A method for inducing myelination of a neuronal cell by a glial cell, comprising contacting said glial cell with a NRG-2 polypeptide, said contacting sufficient to induce myelination of said neuronal cell by said glial cell.

11. A method of increasing the cardiomyocyte survival, cardiomyocyte proliferation, cardiomyocyte growth, or cardiomyocyte differentiation in a mammal in need thereof, said method comprising administering a NRG-2 polypeptide to said mammal in an amount effective for increasing said cardiomyocyte survival, cardiomyocyte proliferation, cardiomyocyte growth, or cardiomyocyte differentiation.

12. The method of claim 11, wherein said mammal is a human.

13. The method of claim 11, wherein said mammal has a pathophysiological condition which affects cardiac muscle.

14. The method of claim 13, wherein said condition is cardiomyopathy or ischemic damage.

15. The method of claim 14, wherein said cardiomyopathy is a degenerative congenital disease.

16. The method of claim 13, wherein said condition is cardiac trauma or heart failure.

17. The method of claim 11, wherein said mammal has a pathophysiological condition which affects smooth muscle.

18. The method of claim 17, wherein said condition is selected from the group consisting of atherosclerosis, vascular lesion, vascular hypertension, and degenerative congenital vascular disease.

19. The method of claim 11, wherein said mammal is a patient with myasthenia gravis.

20. A method of affecting cellular communication between a neuronal-associated cell and a neuronal cell in a mammal, comprising administering a NRG-2 polypeptide to said mammal wherein said neuregulin interacts with said neuronal-associated cell, resulting in the production of at least one neurotrophic agent by said neuronal-associated cell, and said neurotrophic agent or agents affect the mitogenesis, survival, growth, differentiation, or neurite outgrowth of said neuronal cell.

21. The method of claim 20, wherein said mammal is a human.

22. The method of claim 20, wherein said neuronal-associated cell is selected from the group consisting of a Schwann cell, an astrocyte, an oligodendrocyte, an O-2A progenitor cell, a glial cell, an olfactory bulb ensheathing cell, a microglial cell, a sensory organ cell, and a muscle cell.

23. The method of claim 22, wherein said muscle cell is selected from the group consisting of a skeletal muscle cell, a smooth muscle cell, and a cardiac muscle cell.

24. The method of claim 20, wherein said affecting cellular communication is in the central nervous system of a mammal.

25. The method of claim 20, wherein said affecting cellular communication is in the peripheral nervous system of a mammal.

26. The method of claim 20, wherein said administering comprises administering a purified NRG-2 polypeptide-producing cell.

27. A method for the treatment or prophylaxis of a pathophysiological condition of the nervous system in a mammal, said method comprising administering a therapeutically effective amount of a recombinant NRG-2 polypeptide to said mammal.

28. The method of claim 27, wherein said pathophysiological condition is a condition of the peripheral nervous system.

29. The method of claim 27, wherein said pathophysiological condition is a condition of the central nervous system.

30. The method of claim 27, wherein said pathophysiological condition is selected from the group consisting of demyelination of nerve cells, damage of Schwann cells, loss of Schwann cells, and a neurodegenerative disorder.

31. The method of claim 27, wherein said pathophysiological condition is a peripheral neuropathy.

32. The method of claim 31, wherein said neuropathy is a sensory nerve fiber neuropathy.

33. The method of claim 31, wherein said neuropathy is a motor fiber and a sensory nerve fiber neuropathy.

34. The method of claim 31, wherein said neuropathy is a motor fiber neuropathy.

35. The method of claim 27, wherein said treatment or prophylaxis requires neural regeneration or neural repair.

36. The method of claim 27, wherein said pathophysiological condition is multiple sclerosis.

37. The method of claim 27, wherein said pathophysiological condition is selected from the group consisting of amyotrophic lateral sclerosis, spinal muscular atrophy, nerve injury, Alzheimer's Disease, Parkinson's Disease, cerebellar ataxia, and spinal cord injury.

38. The method of claim 27, wherein said NRG-2 polypeptide interacts with neuronal-associated cells, resulting in production of at least one neurotrophic agent by said neuronal-associated cells and said neurotrophic agent or agents affect the mitotic activity, survival, differentiation or neurite outgrowth of neuronal cells.

39. The method of claim 27, wherein said administering is sufficient to induce myelination of a neuronal cell by a glial cell.

40. The method of claim 39, wherein said glial cell is a Schwann cell or an oligodendrocyte.

41. The method of claim 27, wherein said administering comprises administering a purified NRG-2 polypeptide-producing cell to said mammal.

42. The method of claim 26 or 41, wherein said NRG-2 polypeptide-producing cell contains a recombinant DNA sequence, wherein said DNA sequence comprises a NRG-2 polypeptide-encoding sequence, and wherein said NRG-2 polypeptide-encoding DNA sequence is operably linked to a promoter.

43. A method for the treatment of a tumor, said method comprising inhibiting proliferation of a tumor cell, said inhibiting comprising administering to a subject in need thereof an effective amount of an antibody that inhibits binding of a NRG-2 polypeptide to a receptor present on the surface of said tumor cell.

44. The method of claim 43, wherein said tumor cell expresses an erbB receptor that is selective for a NRG-2 polypeptide.

45. The method of claim 43, wherein said tumor is a glial tumor.

46. A method for the treatment of neurofibromatosis, said method comprising inhibiting glial cell mitogenesis, said inhibiting comprising administering to a subject in need thereof an effective amount of an antibody which inhibits binding of a NRG-2 polypeptide to a receptor present on the surface of a glial tumor cell in an individual with neurofibromatosis.

47. A method for inhibiting proliferation of a cell, said method comprising contacting said cell with an effective amount of an antibody that inhibits binding of a NRG-2 polypeptide to a receptor present on the surface of said cell.

48. A method for stimulating proliferation of a cell, said method comprising administering a NRG-2 polypeptide to said cell.

49. The method of claims 47 and 48, wherein said cell is selected from the group consisting of a neuronal cell, a neuronal-associated cell, and a muscle cell.

50. The method of claims 1, 8, 10, 11, 20, 27, 43, 46, 47, and 48, wherein said NRG-2 polypeptide comprises the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

51. The method of claims 1, 8, 10, 11, 20, 27, 43, 46, 47, and 48, wherein said NRG-2 polypeptide consists of the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

52. The method of claims 1, 8, 10, 11, 20, 27, 43, 46, 47, and 48, wherein said NRG-2 polypeptide is encoded by the nucleic acid sequence set forth in SEQ ID NOs: 1 or 3.

53. A substantially pure NRG-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

54. A substantially pure NRG-2 polypeptide consisting of the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

55. A substantially pure nucleic acid molecule comprising a sequence encoding a polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

56. A substantially pure nucleic acid molecule comprising a nucleic acid sequence that is substantially identical to the nucleic acid sequence set forth in SEQ ID NOs: 1 or 3.

57. A substantially pure nucleic acid molecule consisting of the nucleic acid sequence set forth in SEQ ID NOs: 1 or 3.

58. A nucleic acid molecule comprising a sequence that is antisense to the coding strand sequence of the nucleic acid sequence set forth in SEQ ID NOs: 1 or 3, or a fragment thereof.

59. A vector comprising the nucleic acid molecule of claim 55, operably linked to a promoter.

60. The vector of claim 59, wherein said vector is a gene therapy vector.

61. A cell comprising the vector of claim 60.

62. A non-human transgenic animal comprising the nucleic acid molecule of claim 55.

63. A non-human animal having a knockout mutation in one or both alleles encoding the NRG-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

64. A cell from the non-human animal of claim 63.

65. An antibody that specifically binds to a NRG-2 polypeptide comprising the amino acid sequence set forth in SEQ ID NOs: 2 or 4.

66. A method of detecting the presence of a NRG-2 polypeptide in a sample, said method comprising contacting said sample with the antibody of claim 65 and assaying for binding of said antibody to said polypeptide.

67. A method of diagnosing an increased likelihood of developing a NRG-2-related disease or condition in a test subject, said method comprising analyzing nucleic acid molecules of said test subject to determine whether said test subject contains a mutation in NRG-2 gene that encodes a NRG-2 polypeptide comprising the amino acid sequence set forth in SEQ ID Nos: 2 or 4, wherein the presence of said mutation is an indication that said test subject has an increased likelihood of developing a NRG-2-related disease.

68. The method of claim 67, wherein said test subject is human.

69. A kit for the analysis of a NRG-2 polypeptide of a test subject, said kit comprising the antibody of claim 65.